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NEWS 12	FEB 02	GENBANK enhanced with SET PLURALS and SET SPELLING
NEWS 13	FEB 06	Patent sequence location (PSL) data added to USGENE
NEWS 14	FEB 10	COMPENDEX reloaded and enhanced
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NEWS 16	FEB 19	New patent-examiner citations in 300,000 CA/CAplus patent records provide insights into related prior art
NEWS 17	FEB 19	Increase the precision of your patent queries -- use terms from the IPC Thesaurus, Version 2009.01
NEWS 18	FEB 23	Several formats for image display and print options discontinued in USPATFULL and USPAT2
NEWS 19	FEB 23	MEDLINE now offers more precise author group fields and 2009 MeSH terms
NEWS 20	FEB 23	TOXCENTER updates mirror those of MEDLINE - more precise author group fields and 2009 MeSH terms
NEWS 21	FEB 23	Three million new patent records blast AEROSPACE into STN patent clusters
NEWS 22	FEB 25	USGENE enhanced with patent family and legal status display data from INPADOCDB
NEWS 23	MAR 06	INPADOCDB and INPAFAMDB enhanced with new display formats
NEWS 24	MAR 11	EPFULL backfile enhanced with additional full-text applications and grants
NEWS 25	MAR 11	ESBIOBASE reloaded and enhanced

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=> E "THALIDOMIDE"/CN 25
E1            1     THALIDICINE/CN
E2            1     THALIDINE/CN
E3            1 --> THALIDOMIDE/CN
E4            1     THALIDOMIDE-ASPIRIN MIXT./CN
E5            1     THALIDOMIDE-INDOMETHACIN MIXT./CN
E6            1     THALIDOMIDE-PREDNISOLONE MIXT./CN
E7            1     THALIDOMIDE-PREDNISONE MIXT./CN
E8            1     THALIDOXINE/CN
E9            1     THALIDOXINE ACETATE/CN
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E11           1     THALIFABERIDINE/CN
E12           1     THALIFABERINE/CN
E13           1     THALIFABINE/CN
E14           1     THALIFABOMINE/CN
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E15          1     THALIFABORAMINE/CN
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E17          1     THALIFARAMINE/CN
E18          1     THALIFARAPINE/CN
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E22          1     THALIFAROLINE/CN
E23          1     THALIFARONINE/CN
E24          1     THALIFASINE/CN
E25          1     THALIFASINE DIACETATE/CN

=> S E3
L1           1 THALIDOMIDE/CN

=> DIS L1 1 SQIDE

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2009 ACS on STN
RN   50-35-1  REGISTRY
CN   1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)-  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Phthalimide, N-(2,6-dioxo-3-piperidyl)- (6CI, 7CI, 8CI)
OTHER NAMES:
CN   (±)-Thalidomide
CN   α-(N-Phthalimido)glutarimide
CN   α-N-Phthalylglutaramide
CN   α-Phthalimidoglutarimide
CN   1,3-Dioxo-2-(2,6-dioxopiperidin-3-yl)isoindoline
CN   3-Phthalimidoglutarimide
CN   Celgene
CN   Contergan
CN   Distaval
CN   K 17
CN   Kevadon
CN   Myrin
CN   N-(2,6-Dioxo-3-piperidyl)phthalimide
CN   N-Phthaloylglutamimide
CN   Neurosedyn
CN   NSC 527179
CN   NSC 66847
CN   Pantosediv
CN   Pharmion
CN   Quetimid
CN   Sauramide
CN   Sedalis
CN   Sedoval
CN   Softenil
CN   Softenon
CN   Suaramide
CN   Talimol
CN   Talinol
CN   Thalidomide
CN   Thalomid
DR   14088-68-7, 731-40-8
MF   C13 H10 N2 O4
CI   COM
LC   STN Files:   ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*,
       BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST,
       CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IMSCOSEARCH, IMSDRUGNEWS,
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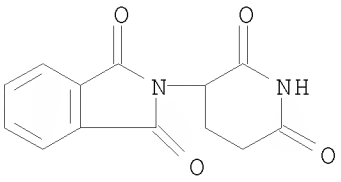
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)



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=> s l1
L2 8229 L1

=> s l2 and (?cancer? or ?tumor? or ?tumour? or ?neoplasm? or ?leukem? or ?lymphoma?)

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L3        3805 L2 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM? OR ?LEUKEM
               ? OR ?LYMPHOMA?)

=> s l3 and (prd<19930301 or pd<19930301)
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L4         125 L3 AND (PRD<19930301 OR PD<19930301)

=> s l4 and (treat? or administ?)
L5          48 L4 AND (TREAT? OR ADMINIST?)

=> d l5 1-48 ibib, abs

L5   ANSWER 1 OF 48     MEDLINE on STN
ACCESSION NUMBER:   1994232213     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 8177242
TITLE:              Inhibition of tumor necrosis factor-alpha by
                    thalidomide in magnesium deficiency.
AUTHOR:             Weglicki W B; Stafford R E; Dickens B F; Mak I T; Cassidy M
                    M; Phillips T M
CORPORATE SOURCE:   Department of Medicine, George Washington University
                    Medical Center, Washington, DC 20037.
CONTRACT NUMBER:    P01-HL-38079 (United States NHLBI NIH HHS)
                    R01-49232 (United States PHS HHS)
SOURCE:             Molecular and cellular biochemistry, (1993 Dec 22)
                    Vol. 129, No. 2, pp. 195-200.
                    Journal code: 0364456. ISSN: 0300-8177.
PUB. COUNTRY:       Netherlands
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
                    (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals; AIDS
ENTRY MONTH:        199406
ENTRY DATE:         Entered STN: 20 Jun 1994
                    Last Updated on STN: 20 Jun 1994
                    Entered Medline: 7 Jun 1994
AB   The effect of thalidomide on circulating cytokines and myocardial lesion
     formation was investigated in Mg-deficient rats.  After two weeks on a
     Mg-deficient diet, rats show an increase in circulating levels of
     tumor necrosis factor-alpha and interleukin 1.  Thalidomide (1
     mg/day) caused a complete inhibition of the increase in circulating
     tumor necrosis factor-alpha levels, without having an effect on
     interleukin 1.  However, a marked increase in cardiomyopathic lesion
     formation was observed in Mg-deficient animals treated with
     thalidomide; possible mechanisms for thalidomide's enhancement of
     myocardial injury are discussed.

L5   ANSWER 2 OF 48     MEDLINE on STN
ACCESSION NUMBER:   1993360618     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 8355553
TITLE:              [Treatment with thalidomide and production of
                    tumor necrosis factor alpha].
                    Terapeutica con talidomida y produccion del factor de
                    necrosis tumoral alfa.
AUTHOR:             Pizarro A; Pinilla J; Garcia-Tobaruela A
SOURCE:             Medicina clinica, (1993 Jun 19) Vol. 101, No. 4,
                    pp. 158.
                    Journal code: 0376377. ISSN: 0025-7753.
PUB. COUNTRY:       Spain
DOCUMENT TYPE:      Commentary
                    Letter
LANGUAGE:           Spanish
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FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 8 Oct 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 17 Sep 1993

L5 ANSWER 3 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1993329195 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8335978
TITLE: The influence of thalidomide on the clinical and immunologic manifestation of erythema nodosum leprosum.
AUTHOR: Sampaio E P; Kaplan G; Miranda A; Nery J A; Miguel C P; Viana S M; Sarno E N
CORPORATE SOURCE: Leprosy Unit, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil.
CONTRACT NUMBER: AI-22616 (United States NIAID NIH HHS)
SOURCE: The Journal of infectious diseases, (1993 Aug) Vol. 168, No. 2, pp. 408-14.
Journal code: 0413675. ISSN: 0022-1899.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199308
ENTRY DATE: Entered STN: 3 Sep 1993
Last Updated on STN: 3 Sep 1993
Entered Medline: 24 Aug 1993

AB Immunologic and clinical manifestations of erythema nodosum leprosum (ENL) and their response to thalidomide therapy were evaluated. Circulating tumor necrosis factor-alpha (TNF alpha) levels were assayed in serum obtained from lepromatous leprosy patients at diagnosis, during multidrug therapy, at the onset of ENL episodes, and during treatment with thalidomide. Patients with systemic ENL demonstrated the highest serum TNF alpha levels, which decreased significantly during thalidomide treatment. Serum TNF alpha in nonreactional patients was associated with mild flu-like symptoms and local inflammatory lesions. Serum interferon-gamma (IFN-gamma) was also elevated in patients with high TNF alpha levels. Thalidomide therapy reduced not only serum TNF alpha levels and the clinical symptoms but also the dermal infiltration of polymorphonuclear leukocytes and T cells. The expression of intercellular adhesion molecule 1 and major histocompatibility complex class II antigens on the epidermal keratinocytes was also down-regulated. These results indicate that the thalidomide-induced alleviation of clinical symptoms of ENL was associated with a reduction of TNF alpha levels.

L5 ANSWER 4 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1993267219 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8496685
TITLE: Thalidomide exerts its inhibitory action on tumor necrosis factor alpha by enhancing mRNA degradation.
AUTHOR: Moreira A L; Sampaio E P; Zmuidzinas A; Frindt P; Smith K A; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (United States NIAID NIH HHS)
AI-33124 (United States NIAID NIH HHS)
SOURCE: The Journal of experimental medicine, (1993 Jun 1) Vol. 177, No. 6, pp. 1675-80.
Journal code: 2985109R. ISSN: 0022-1007.

Report No.: NLM-PMC2191046.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199306
ENTRY DATE: Entered STN: 2 Jul 1993
Last Updated on STN: 2 Jul 1993
Entered Medline: 21 Jun 1993

AB We have examined the mechanism of thalidomide inhibition of lipopolysaccharide (LPS)-induced tumor necrosis factor alpha (TNF-alpha) production and found that the drug enhances the degradation of TNF-alpha mRNA. Thus, the half-life of the molecule was reduced from approximately 30 to approximately 17 min in the presence of 50 micrograms/ml of thalidomide. Inhibition of TNF-alpha production was selective, as other LPS-induced monocyte cytokines were unaffected. Pentoxifylline and dexamethasone, two other inhibitors of TNF-alpha production, are known to exert their effects by means of different mechanisms, suggesting that the three agents inhibit TNF-alpha synthesis at distinct points of the cytokine biosynthetic pathway. These observations provide an explanation for the synergistic effects of these drugs. The selective inhibition of TNF-alpha production makes thalidomide an ideal candidate for the treatment of inflammatory conditions where TNF-alpha-induced toxicities are observed and where immunity must remain intact.

L5 ANSWER 5 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1993226612 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8469665
TITLE: [Sclerodermatous cutaneous reaction of graft vs host disease treated with thalidomide].
Reaction cutanee sclerodermiforme du greffon contre l'hote traitee par thalidomide.
AUTHOR: Pedailles S; Troussard X; Launay V; Bazin A; Sentias C; Surbled M
SOURCE: Presse medicale (Paris, France : 1983), (Jan 2-16 1993) Vol. 22, No. 1, pp. 37.
Journal code: 8302490. ISSN: 0755-4982.
PUB. COUNTRY: France
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: French
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199305
ENTRY DATE: Entered STN: 21 May 1993
Last Updated on STN: 21 May 1993
Entered Medline: 12 May 1993

L5 ANSWER 6 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1993020249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1403704
TITLE: Improvements in solubility and stability of thalidomide upon complexation with hydroxypropyl-beta-cyclodextrin.
AUTHOR: Krenn M; Gamcsik M P; Vogelsang G B; Colvin O M; Leong K W
CORPORATE SOURCE: Department of Biomedical Engineering, Johns Hopkins University, Baltimore, MD 21218.
CONTRACT NUMBER: CA44783 (United States NCI NIH HHS)
SOURCE: Journal of pharmaceutical sciences, (1992 Jul) Vol. 81, No. 7, pp. 685-9.
Journal code: 2985195R. ISSN: 0022-3549.

PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199211
ENTRY DATE: Entered STN: 22 Jan 1993
Last Updated on STN: 22 Jan 1993
Entered Medline: 10 Nov 1992

AB Thalidomide is in clinical use for the treatment of graft-versus-host disease in leukemia patients after bone marrow transplant. Low levels of the drug in plasma after oral administration have made an intravenous thalidomide formulation desirable. Thalidomide, however, is sparingly soluble in aqueous solution (50 micrograms/mL) and unstable. Complexation with hydroxypropyl-beta-cyclodextrin has significantly improved the aqueous solubility and stability of thalidomide. Results obtained with HPLC and 1H NMR spectrometry have demonstrated that the solubility is increased to 1.7 mg/mL and the half-life of a diluted solution is extended from 2.1 to 4.1 h. Hence, an intravenous thalidomide-hydroxypropyl- beta-cyclodextrin solution has the potential to significantly improve current therapy for graft-versus-host disease by providing sustained high levels of drug in the plasma.

L5 ANSWER 7 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1992268822 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1588290
TITLE: Prolonged treatment with recombinant interferon gamma induces erythema nodosum leprosum in lepromatous leprosy patients.
AUTHOR: Sampaio E P; Moreira A L; Sarno E N; Malta A M; Kaplan G
CORPORATE SOURCE: Laboratory of Cellular Physiology and Immunology, Rockefeller University, New York, New York 10021.
CONTRACT NUMBER: AI-22616 (United States NIAID NIH HHS)
SOURCE: The Journal of experimental medicine, (1992 Jun 1) Vol. 175, No. 6, pp. 1729-37.
Journal code: 2985109R. ISSN: 0022-1007.
Report No.: NLM-PMC2119233.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199206
ENTRY DATE: Entered STN: 10 Jul 1992
Last Updated on STN: 10 Jul 1992
Entered Medline: 23 Jun 1992

AB 10 patients with borderline and lepromatous leprosy were selected for a prolonged trial with recombinant interferon gamma (rIFN-gamma). Patients received 30 micrograms intradermally for six injections over a 9-d period, and then either 100 micrograms intradermally every 1 mo for 10 mo or every 2 wk for 5 mo (total, 1.2 mg). Erythema nodosum leprosum (ENL) was induced in 60% of the patients within 6-7 mo, as compared with an incidence of 15% per year with multiple drug therapy alone. The mean whole-body reduction in bacterial index over the first 6 mo was 0.9 log units. Cutaneous induration at the intradermal injection sites of greater than or equal to 15 mm predicted the development of a subsequent reactional state. Monocytes obtained from patients receiving the lymphokine demonstrated an increased respiratory burst and a 2.5-5.1-fold

increase in tumor necrosis factor alpha (TNF-alpha) secretion in response to agonists. Patients in ENL had an even higher release of TNF-alpha from monocytes as well as high levels of TNF-alpha in the plasma (mean, 2,000 pg/ml). Thalidomide therapy was required to treat the systemic manifestations of ENL. Control of toxic symptoms with thalidomide was associated with a 50-80% reduction in agonist-stimulated monocyte TNF-alpha secretion. IFN-gamma enhanced the monocyte release of TNF-alpha by 3-7.5-fold (agonist dependent) when added to patient's cells in vitro, and this could be suppressed by the in vitro addition of 10 micrograms/ml of thalidomide.

L5 ANSWER 8 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1992195361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1549151
TITLE: Thalidomide for the treatment of chronic graft-versus-host disease.
AUTHOR: Vogelsang G B; Farmer E R; Hess A D; Altamonte V; Beschorner W E; Jabs D A; Corio R L; Levin L S; Colvin O M; Wingard J R; et al
CORPORATE SOURCE: Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Md.
CONTRACT NUMBER: CA-15396 (United States NCI NIH HHS)
R01-CA-44783 (United States NCI NIH HHS)
SOURCE: The New England journal of medicine, (1992 Apr 16) Vol. 326, No. 16, pp. 1055-8.
Journal code: 0255562. ISSN: 0028-4793.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199204
ENTRY DATE: Entered STN: 9 May 1992
Last Updated on STN: 9 May 1992
Entered Medline: 21 Apr 1992

AB BACKGROUND. Allogeneic bone marrow transplantation is an accepted therapy for hematologic cancer, aplastic anemia, and inherited immunodeficiencies. Chronic graft-versus-host disease (GVHD) is the principal complication in patients surviving more than 100 days. Thalidomide has been shown experimentally to be effective in treating GVHD. METHODS. We treated 23 patients with chronic GVHD refractory to conventional treatment and 21 patients with "high-risk" chronic GVHD (identified as having at least two of the following three risk factors: chronic GVHD that has evolved from acute GVHD, lichenoid skin or mucous-membrane changes, and hepatic dysfunction. Such patients have a high mortality rate.) with thalidomide in a dose that produced a plasma level of 5 micrograms per milliliter two hours after administration. Therapy was continued for three months after a complete response or for six months after a partial response. RESULTS. The overall actuarial survival of all enrolled patients was 64 percent. Survival was 76 percent among the patients receiving salvage therapy for refractory GVHD and 48 percent among those with high-risk GVHD. A complete response was observed in 14 patients, a partial response in 12 patients, and no response in 18. Side effects were minor, most notably sedation in almost all patients. CONCLUSIONS. In this preliminary trial, thalidomide appeared to be safe and effective for the treatment of chronic GVHD. A trial comparing thalidomide with prednisone in patients with newly diagnosed chronic GVHD will be required to demonstrate its relative efficacy.

L5 ANSWER 9 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1992034660 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1933837
TITLE: The thalidomide analog, EM 12, enhances 1,2-dimethylhydrazine-induction of rat colon adenocarcinomas.
AUTHOR: Gershbein L L
CORPORATE SOURCE: Biochemistry and Oncology Sections, Northwest Institute for Medical Research, John F. Kennedy Health Care Corporation, Chicago, Illinois 60645.
SOURCE: Cancer letters, (1991 Nov) Vol. 60, No. 2, pp. 129-33.
Journal code: 7600053. ISSN: 0304-3835.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199112
ENTRY DATE: Entered STN: 24 Jan 1992
Last Updated on STN: 6 Feb 1998
Entered Medline: 2 Dec 1991
AB Young male Sprague-Dawley rats in 3 groups were fed a basal diet supplemented with 0.10 weight % each of thalidomide and its imide-analog of much higher teratogenicity, EM 12. Following an induction period of 17 days on the diets, all animals were injected subcutaneously with 1,2-dimethylhydrazine at 20 mg/kg for a total of 20 weekly doses and killed on week 18 after the 20th injection. The total number of colon adenocarcinomas and their occurrence in the proximal and distal portions for the thalidomide-treated rats were similar to those of the respective controls. However, the EM 12-fed group elicited statistically significant increases both in the total and ascending colon-based adenocarcinomas as compared with the control findings, in keeping with its greater teratogenicity and embryotoxicity. The numbers of small intestinal adenocarcinomas were equally higher in the imide-fed groups in contrast to the control frequency.

L5 ANSWER 10 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1988093229 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2891954
TITLE: Successful treatment with thalidomide of acute graft-versus-host disease after bone-marrow transplantation.
AUTHOR: Lim S H; McWhannell A; Vora A J; Boughton B J
SOURCE: Lancet, (1988 Jan 16) Vol. 1, No. 8577, pp. 117.
Journal code: 2985213R. ISSN: 0140-6736.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CASE REPORTS)
Letter
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 198802
ENTRY DATE: Entered STN: 5 Mar 1990
Last Updated on STN: 6 Feb 1995
Entered Medline: 17 Feb 1988

L5 ANSWER 11 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1986123775 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3945939
TITLE: Teratogen metabolism: thalidomide activation is mediated by cytochrome P-450.
AUTHOR: Braun A G; Harding F A; Weinreb S L

SOURCE: Toxicology and applied pharmacology, (1986 Jan)
Vol. 82, No. 1, pp. 175-9.
Journal code: 0416575. ISSN: 0041-008X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 198603
ENTRY DATE: Entered STN: 21 Mar 1990
Last Updated on STN: 21 Mar 1990
Entered Medline: 4 Mar 1986

AB A metabolite of thalidomide generated by hepatic microsomes inhibited the attachment of tumor cells to concanavalin A-coated polyethylene. Evidence that metabolite formation is mediated by microsomal cytochrome P-450 is presented. Microsomes incubated with thalidomide underwent a type I spectral shift. Metabolite formation was reduced or eliminated by carbon monoxide, SKF-525A, metyrapone, and N-octylamine. Superoxide dismutase treatment had no effect. Metabolite formation required microsomes and NADPH and was dependent on the length of 37 degrees C incubation. The metabolite could be isolated by successive hexane and chloroform extractions. It is likely the inhibitory thalidomide metabolite was generated by a minor cytochrome P-450 species. Whether this thalidomide metabolite is involved in the drug's teratogenic activity remains to be shown.

L5 ANSWER 12 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1983136405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7161406
TITLE: The use of vital and morbidity statistics for the detection of adverse drug reactions and for monitoring of drug safety.
AUTHOR: Stolley P D
SOURCE: Journal of clinical pharmacology, (1982 Nov-Dec)
Vol. 22, No. 11-12, pp. 499-504.
Journal code: 0366372. ISSN: 0091-2700.
Report No.: PIP-015015; POP-00119443.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population; AIDS
ENTRY MONTH: 198304
ENTRY DATE: Entered STN: 18 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 7 Apr 1983

AB Several examples of the use of vital statistics in drug epidemiology are described. The death rates for asthma remained stable from about 1860-1960 in the UK, about 0.5/100,000. In 1961 the rates began to rise, and after 1967 they declined; in the 1970s the rates almost approached pre-epidemic levels. The rates were found to vary with the use of isoproterenol-containing nebulizers. Investigations into the relationship between thromboembolism pulmonary embolism, and myocardial infarction and oral contraceptive (OC) usage showed an increase in death rates beginning after the introduction of OCs in 1960-61 in women at risk. Subacute myelo-optic neuropathy was an unexplained disease until Japanese investigators linked its occurrence to ingestion of the halogenated hydroxyquinoline drugs used to treat nonspecific gastroenteritis; seasonal outbreaks of the disease were linked to seasonal gastroenteritis. Animal experiments conclusively linked the drug to the disease. A Swedish report implicated the antihypertensive drug methyldopa as a possible cause of cancer of the biliary ducts. Links

between thalidomide and phocomelia, saccharin or cyclamates and bladder cancer, diethylstilbestrol and vaginal cancer, and estrogens and endometrial cancer are discussed. Drug-monitoring systems, the collection of vital statistics and observations by clinicians all contribute to understanding drug-induced disease. Changes in disease incidence or emergency of new syndromes in areas where certain drugs are heavily used should be compared to areas where they are seldom used.

L5 ANSWER 13 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1979178458 MEDLINE
DOCUMENT NUMBER: PubMed ID: 440336
TITLE: Necessary risks.
AUTHOR: Jarvik M E
SOURCE: The New England journal of medicine, (1979 Jun 7) Vol. 300, No. 23, pp. 1330.
Journal code: 0255562. ISSN: 0028-4793.
PUB. COUNTRY: United States
DOCUMENT TYPE: Editorial
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197907
ENTRY DATE: Entered STN: 15 Mar 1990
Last Updated on STN: 15 Mar 1990
Entered Medline: 16 Jul 1979

L5 ANSWER 14 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1975070562 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4140679
TITLE: Human experiences related to adverse drug reactions to the fetus or neonate from some maternally administered drugs.
AUTHOR: Shirkey H C
SOURCE: Advances in experimental medicine and biology, (1972) Vol. 27, pp. 17-30.
Journal code: 0121103. ISSN: 0065-2598.
Report No.: PIP-723949; POP-00015296.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Population
ENTRY MONTH: 197503
ENTRY DATE: Entered STN: 10 Mar 1990
Last Updated on STN: 1 Nov 2002
Entered Medline: 17 Mar 1975

AB This is a review of known periods in utero during which drugs alter the process of growth; effects may be shown on the fetus or the newborn and vary with the stage of development of the fetus when exposed. Other variables are the mother and the placenta. There is no safe animal screening mechanism, the human test is by ordeal, and more clinical monitoring and reporting are needed. Cancer chemotherapeutic agents exert their maximal effects on rapidly dividing cells and are therefore hazardous during pregnancy; the greatest risk is in the 1st trimester. In the thalidomide experience the critical days were the 22nd and 23rd days after conception. Masculinizing drugs such as testosterone and other androgenic steroids have been implicated as affecting the female fetus when given early in pregnancy. Oral contraceptives taken by an already pregnant woman are a hazard because of these progestational agents. Progesterone alone is unlikely to cause masculinization but other progestins may cause such changes. Carcinogenesis may develop later in females born of mothers who are treated with diethylstilbestrol to prevent miscarriage. Many antithyroid drugs have caused neonatal goiter. Maternal ingestion of iodides during pregnancy (preparations for

treating asthma, cough syrups, radio-contrast media used in diagnoses) is the most frequent cause. Goiter is relatively common in infants whose mothers were treated with propylthiouracil and other antithyroid drugs, yet they usually show normal thyroid function. However, hypothyroidism with cretinism can occur. Lithium, used in psychiatry and as a salt substitute, may alter iodine metabolism and thyroid gland function. It also passes into the milk to continue the potential toxicity. Teratogenic effects in experimental animals suggest other possible effects on infants from lithium and similar drugs.

L5 ANSWER 15 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1971133848 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5401721
TITLE: [Immunodepressive action of thalidomide and prednisolone in rats with experimentally induced neoplasms].
Ricerche sull'azione immunodepressiva della talidomide e del prednisolone in ratti portatori di neoplasie sperimentalmente indotte.
AUTHOR: Guidetti E; Moiraghi-Ruggenini A; Errigo E; Martelli M P
SOURCE: Il Cancro, (1969) Vol. 22, No. 5, pp. 503-12.
Journal code: 0421125. ISSN: 0008-5480.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197104
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 25 Apr 1971

L5 ANSWER 16 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1968326790 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5631600
TITLE: [Treatment of a 2nd degree astrocytoma with thalidomide (N-phthalylglutamic acid amide].
Behandlung eines Astrocytomas II. Grades mit Thalidomid (N-Phthalylglutaminsaureimid).
AUTHOR: Buelens I
SOURCE: Arzneimittel-Forschung, (1967 May) Vol. 17, No. 5, pp. 646-8.
Journal code: 0372660. ISSN: 0004-4172.
PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196809
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 6 Sep 1968

L5 ANSWER 17 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1968274900 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6014810
TITLE: [Clinical observations in the influence of thalidomide in the treatment of a leiomyoma in a dog].
Klinische Beobachtung uber den Einfluss von Thalidomid bei der Behandlung eines Leiomyoms bei einem Hund.
AUTHOR: Zwart D
SOURCE: Arzneimittel-Forschung, (1966 Dec) Vol. 16, No. 12, pp. 1688-9.
Journal code: 0372660. ISSN: 0004-4172.

PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196807
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 29 Jul 1968

L5 ANSWER 18 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1967176011 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4291111
TITLE: Tumour-incidence in progeny of thalidomide-treated mice.
AUTHOR: Roe F J; Walters M A; Mitchley B C
SOURCE: British journal of cancer, (1967 Jun) Vol. 21, No. 2, pp. 331-3.
Journal code: 0370635. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196709
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 6 Feb 1998
Entered Medline: 2 Sep 1967

L5 ANSWER 19 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1966169692 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5887938
TITLE: [Use of the imide of N-phthalylglutamic acid (thalidomide) in the symptomatic therapy of vomiting of many patients with malignant neoplasms or caused by the administration of mechlorethamine HCl].
L'impiego dell'imide dell'acido N-ftalilglutammico (talidomide) nella terapia sintomatica del vomito di molti pazienti affetti da neoplasie maligne o causato dalla somministrazione di cloridato di mecloretamina.
AUTHOR: Traldi A; Vaccari G L; Davoli G
SOURCE: Il Cancro, (1965) Vol. 18, No. 4, pp. 336-41.
Journal code: 0421125. ISSN: 0008-5480.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196610
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 16 Oct 1966

L5 ANSWER 20 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1966110143 MEDLINE
DOCUMENT NUMBER: PubMed ID: 4956141
TITLE: Carcinogenesis in tissue culture. 3. Effects of the second treatments on DAB-induced proliferating liver cells of normal rats in culture.
AUTHOR: Katsuta H; Takaoka T
SOURCE: The Japanese journal of experimental medicine, (1965 Aug) Vol. 35, No. 4, pp. 231-48.
Journal code: 9800765. ISSN: 0021-5031.
PUB. COUNTRY: Japan
DOCUMENT TYPE: (IN VITRO)

Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 196606
ENTRY DATE: Entered STN: 1 Jan 1990
Last Updated on STN: 1 Jan 1990
Entered Medline: 25 Jun 1966

L5 ANSWER 21 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1965100632 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14296025
TITLE: THALIDOMIDE (N-PHTHALOYLGLUTAMIMIDE) IN THE TREATMENT OF ADVANCED CANCER.
AUTHOR: OLSON K B; HALL T C; HORTON J; KHUNG C L; HOSLEY H F
SOURCE: Clinical pharmacology and therapeutics, (1965 May-Jun) Vol. 6, pp. 292-7.
Journal code: 0372741. ISSN: 0009-9236.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 22 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1964081361 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14123612
TITLE: [TREATMENT OF EXPERIMENTAL TUMORS WITH THALIDOMIDE].
TRATTAMENTO DI TUMORI SPERIMENTALI CON TALIDOMIDE.
AUTHOR: PAGNINI G; DICARLO R
SOURCE: Bollettino della Societa italiana di biologia sperimentale, (1963 Nov 30) Vol. 39, pp. 1360-3.
Journal code: 7506962. ISSN: 0037-8771.
PUB. COUNTRY: Italy
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Italian
FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 23 OF 48 MEDLINE on STN
ACCESSION NUMBER: 1964039115 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14081473
TITLE: [CLINICAL IMPROVEMENTS OBTAINED IN ADVANCED CANCER PATIENTS WITH TREATMENT WITH THALIDOMIDE ASSOCIATED WITH HORMONES].
MELHORAS CL'INICAS OBTIDAS EM DOENTES CANCEROSOS AVAN CADOS COM TRATAMENTO PELA TALIDOMIDA ASSOCIADA A HORM ONIOS.
AUTHOR: MAUAD M J
SOURCE: Anais paulistas de medicina e cirurgia, (1963 Jul) Vol. 86, pp. 13-40.
Journal code: 0373070. ISSN: 0003-245X.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Portuguese

FILE SEGMENT: OLDMEDLINE; NONMEDLINE
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 16 Jul 1999
Last Updated on STN: 16 Jul 1999
Entered Medline: 1 Dec 1996

L5 ANSWER 24 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:41116 CAPLUS
DOCUMENT NUMBER: 140:105248
TITLE: Synthesis and antiproliferative effects of 1α,24(S)-dihydroxyvitamin D2, and use with other agents
INVENTOR(S): Bishop, Charles W.; Knutson, Joyce C.; Strugnell, Stephen; Mazess, Richard B.
PATENT ASSIGNEE(S): Bone Care International, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp., Cont.-in-part of U.S. Pat. Appl. 2002 32,179.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040009958	A1	20040115	US 2003-390953	20030318 <--
WO 9212165	A1	19920723	WO 1992-US313	19920107 <--
W: AU, BR, CA, FI, HU, JP, KP, KR, NO, PL, RU, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				
EP 914825	A2	19990512	EP 1998-110802	19920107 <--
EP 914825	A3	19990519		
EP 914825	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC				
US 5786348	A	19980728	US 1995-477930	19950607 <--
US 5789397	A	19980804	US 1995-485184	19950607 <--
US 6166000	A	20001226	US 1995-472499	19950607
US 6143910	A	20001107	US 1998-211984	19981214 <--
US 6251883	B1	20010626	US 1998-211991	19981214 <--
US 20020032179	A1	20020314	US 2001-891963	20010626
US 6538037	B2	20030325		
CA 2451039	A1	20030109	CA 2002-2451039	20020626
WO 2003002110	A1	20030109	WO 2002-US20317	20020626
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002315463	A1	20030303	AU 2002-315463	20020626
AU 2002315463	B2	20070531		
EP 1408939	A1	20040421	EP 2002-742318	20020626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1520288	A	20040811	CN 2002-812836	20020626
JP 2004535441	T	20041125	JP 2003-508349	20020626
MX 2003011306	A	20040319	MX 2003-11306	20031208
AU 2004222310	A1	20040930	AU 2004-222310	20040316
CA 2517125	A1	20040930	CA 2004-2517125	20040316
WO 2004082631	A2	20040930	WO 2004-US8136	20040316

WO 2004082631 A3 20051229
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 1617810 A2 20060125 EP 2004-749390 20040316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK
BR 2004008468 A 20060404 BR 2004-8468 20040316
CN 1774242 A 20060517 CN 2004-80007470 20040316
JP 2006520791 T 20060914 JP 2006-507271 20040316
PRIORITY APPLN. INFO.: US 1991-637867 B2 19910108 <--
WO 1992-US313 A2 19920107 <--
US 1992-940246 B1 19920828 <--
US 1994-275641 B1 19940714
US 1995-515801 B2 19950816
US 1998-211991 A2 19981214
US 2001-891963 A2 20010626
EP 1992-904947 A3 19920107 <--
WO 2002-US20317 W 20020626
US 2003-390953 A 20030318
WO 2004-US8136 A 20040316

AB The invention discloses the hormonally active, natural metabolite 1α,24(S)-dihydroxyvitamin D2 and a method of preparing this metabolite and the nonbiol. epimer 1α,24(R)-dihydroxyvitamin D2. The invention also relates to a pharmaceutical composition including a pharmaceutically effective amount of 1α,24(S)-dihydroxyvitamin D2, to a method of controlling abnormal calcium metabolism by administering a pharmaceutically effective amount of the compound, and to a method of treating hyperproliferative diseases by administering the compound The method also includes the co-administration of cytotoxic agents with the 1α,24(S)-dihydroxyvitamin D2.

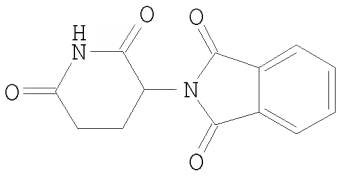
L5 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1994:214219 CAPLUS
DOCUMENT NUMBER: 120:214219
ORIGINAL REFERENCE NO.: 120:37937a,37940a
TITLE: Inhibition of tumor necrosis factor-alpha by thalidomide in magnesium deficiency
AUTHOR(S): Weglicki, William B.; Stafford, Richard E.; Dickens, Benjamin F.; Mak, I. Tong; Cassidy, Marie M.; Phillips, Terry M.
CORPORATE SOURCE: Med. Cent., George Washington Univ., Washington, DC, 20037, USA
SOURCE: Molecular and Cellular Biochemistry (1993), 129(2), 195-200
CODEN: MCBIB8; ISSN: 0300-8177
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of thalidomide on circulating cytokines and myocardial lesion formation was investigated in Mg-deficient rats. After two weeks on a Mg-deficient diet, rats show an increase in circulating levels of tumor necrosis factor-alpha and interleukin 1. Thalidomide (1 mg/day) caused a complete inhibition of the increase in circulating tumor necrosis factor-alpha levels, without having an effect in

interleukin 1. However, a marked increased in cardiomyopathic lesion formation was observed in Mg-deficient animals treated with thalidomide; possible mechanisms for thalidomide's enhancement of myocardial injury are discussed.

L5 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:204908 CAPLUS
DOCUMENT NUMBER: 118:204908
ORIGINAL REFERENCE NO.: 118:34981a,34984a
TITLE: Thalidomide exerts its inhibitory action on tumor necrosis factor α by enhancing mRNA degradation
AUTHOR(S): Moreira, Andre L.; Sampaio, Elizabeth P.; Zmuidzinas, Antonina; Frindt, Paula; Smith, Kendall A.; Kaplan, Gilla
CORPORATE SOURCE: Dep. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1993), 177(6), 1675-80
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The mechanism of thalidomide inhibition of lipopolysaccharide (LPS)-induced tumor necrosis factor α (TNF-α) production was examined; the drug enhanced the degradation of TNF-α mRNA. The half-life of the mol. was reduced from .apprx.30 to .apprx.17 min in the presence of 50 μg/mL of thalidomide. Inhibition of TNF-α production was selective, as other LPS-induced monocyte cytokines were unaffected. Pentoxifylline and dexamethasone, two other inhibitors of TNF-α production, are known to exert their effects by means of different mechanisms, suggesting that the three agents inhibit TNF-α synthesis at distinct points of the cytokine biosynthetic pathway. These observations provide an explanation for the synergistic effects of these drugs. The selective inhibition of TNF-α production makes thalidomide an ideal candidate for the treatment of inflammatory conditions where TNF-α-induced toxicities are observed and where immunity must remain intact.

L5 ANSWER 27 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1993:11605 CAPLUS
DOCUMENT NUMBER: 118:11605
ORIGINAL REFERENCE NO.: 118:2177a,2180a
TITLE: Improvements in solubility and stability of thalidomide upon complexation with hydroxypropyl-β-cyclodextrin
AUTHOR(S): Krenn, Martina; Gamcsik, Michael P.; Vogelsang, Georgia B.; Colvin, O. Michael; Leong, Kam W.
CORPORATE SOURCE: Dep. Biomed. Eng., Johns Hopkins Univ., Baltimore, MD, 21218, USA
SOURCE: Journal of Pharmaceutical Sciences (1992), 81(7), 685-9
CODEN: JPMSAE; ISSN: 0022-3549
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



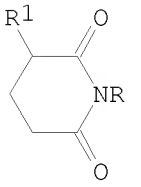
I

AB Thalidomide (I) is in clin. use for the treatment of graft-vs.-host disease in leukemia patients after bone marrow transplant. Low levels of the drug in plasma after oral administration have made an i.v. thalidomide formulation desirable. I, however, is sparingly soluble in aqueous solution (50 μg/mL) and unstable. Complexation with hydroxypropyl β-cyclodextrin (HPβCD) has significantly improved the aqueous solubility and stability of I. Results obtained with HPLC and NMR spectrometry have demonstrated that the solubility is increased to 1.7 mg/mL and the half-life of a dilute solution is extended from 2.1 to 4.1 h. Hence, an i.v. I-HPβCD in solution has the potential to improve current therapy for graft-vs.-host disease by providing sustained high levels of drug in the plasma.

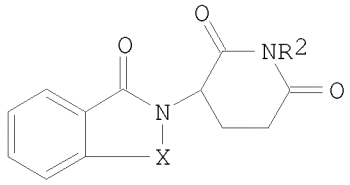
L5 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:626313 CAPLUS
DOCUMENT NUMBER: 117:226313
ORIGINAL REFERENCE NO.: 117:38893a,38896a
TITLE: Controlling abnormal concentration of tumor necrosis factor-α (TNF-α) in human tissues with phthalimido dioxopiperidines and related compounds
INVENTOR(S): Kaplan, Gilla; Sampaio, Elisabeth P.
PATENT ASSIGNEE(S): Rockefeller University, USA
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE	
WO 9214455	A1	19920903	WO 1992-US1207		19920214	<--
W: AU, CA, JP						
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE						
AU 9215314	A	19920915	AU 1992-15314		19920214	<--
US 5385901	A	19950131	US 1992-955936		19921002	<--
PRIORITY APPLN. INFO.:			US 1991-655087	A	19910214	<--
			US 1992-834588	A	19920212	<--
			WO 1992-US1207	A	19920214	<--

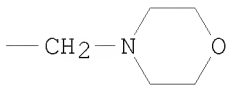
GI



I



II



Q

AB The dioxopiperidine derivs. I (R = H, alkyl, Ph, benzyl; R1 = phthalamide or succinimido radical) and II (X = CH2, CO; R2 = H, Et, Ph, benzyl, CH2CH:CH2, Q) and II hydrolysis products, are drugs for treatment of the debilitating effects of toxic TNF-α levels in humans, such as in septic shock, cachexia and human immunodeficiency virus infection. Thalidomide (2 ng to 10 μg/mL) decreased the tuberculin-stimulated production of TNF-α in human monocytes in vitro. The preparation of thalidomide and 3-phthalimido-2,6-dioxo-1-ethylpiperidine are given.

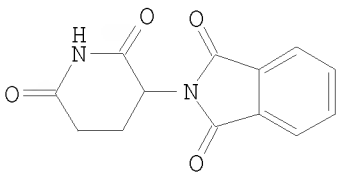
L5 ANSWER 29 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1992:212678 CAPLUS
DOCUMENT NUMBER: 116:212678
ORIGINAL REFERENCE NO.: 116:36015a,36018a
TITLE: Prolonged treatment with recombinant interferon γ induces erythema nodosum leprosum in lepromatous leprosy patients
AUTHOR(S): Sampaio, Elizabeth P.; Moreira, Andre L.; Sarno, Euzenir N.; Malta, Ana M.; Kaplan, Gilla
CORPORATE SOURCE: Lab. Cell. Physiol. Immunol., Rockefeller Univ., New York, NY, 10021, USA
SOURCE: Journal of Experimental Medicine (1992), 175(6), 1729-37
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Patients with borderline and lepromatous leprosy were selected for a prolonged trial with recombinant interferon γ (rIFN-γ). Patients received 30 μg intradermally for 6 injections over a 9-day period, and then either 100 μg intradermally every 1 mo for 10 mo or every 2 wk for 5 mo (total, 1.2 mg). Erythema nodosum leprosum (ENL) was induced in 60% of the patients within 6-7 mo, as compared with an incidence of 15% per yr with multiple drug therapy alone. The mean whole-body reduction in bacterial index over the first 6 mo was 0.9 log units. Cutaneous induration at the intradermal injection sites of ≥15 mm predicted the development of a subsequent reactional state. Monocytes obtained from patients receiving the lymphokine demonstrated an increased respiratory burst and a 2.5-5.1-fold increase in tumor necrosis factor α (TNF-α) secretion in response to agonists. Patients in ENL had an even higher release of TNF-α from monocytes as well as high levels of TNF-α in the plasma (2000 pg/mL). Thalidomide therapy was required to treat the systemic manifestations of ENL. Control of toxic symptoms with thalidomide was associated with a 50-80% reduction in agonist-stimulated monocyte TNF-α secretion. IFN-γ enhanced the monocyte release of TNF-α by 3-7.5-fold (agonist dependent) when added to patient's cells in vitro, and this could be suppressed by the in vitro addition of 10 μg/mL of thalidomide.

L5 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1991:670604 CAPLUS
DOCUMENT NUMBER: 115:270604
ORIGINAL REFERENCE NO.: 115:45745a,45748a

TITLE: The thalidomide analog, EM 12, enhances 1,2-dimethylhydrazine-induction of rat colon adenocarcinomas
AUTHOR(S): Gershbein, Leon L.
CORPORATE SOURCE: Northwest Inst. Med. Res., John F. Kennedy Health Care Corp., Chicago, IL, 60645, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1991), 60(2), 129-33
CODEN: CALEDQ; ISSN: 0304-3835
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Young male rats were fed a basal diet supplemented with 0.10% of thalidomide and its highly teratogenic imide-analog EM-12. Following an induction period of 17 days on the diets, all animals were injected s.c. with 1,2-dimethylhydrazine at 20 mg/kg for a total of 20 doses and killed on wk 18 after the 20th injection. The total number of colon adenocarcinomas and their occurrence in the proximal and distal portions for the thalidomide-treated rats were similar to those of the resp. controls. The EM-12-fed group had increased the total and ascending colon adenocarcinomas as compared with the controls suggesting a greater teratogenicity and embryotoxicity of EM-12. The nos. of small intestinal adenocarcinomas were also higher in the imide-fed groups in contrast to the control frequency.

L5 ANSWER 31 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1986:124742 CAPLUS
DOCUMENT NUMBER: 104:124742
ORIGINAL REFERENCE NO.: 104:19631a,19634a
TITLE: Teratogen metabolism: thalidomide activation is mediated by cytochrome P 450
AUTHOR(S): Braun, Andrew G.; Harding, Fiona A.; Weinreb, Steven L.
CORPORATE SOURCE: Dep. Appl. Biol. Sci., Massachusetts Inst. Technol., Cambridge, MA, 01239, USA
SOURCE: Toxicology and Applied Pharmacology (1986), 82(1), 175-9
CODEN: TXAPA9; ISSN: 0041-008X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

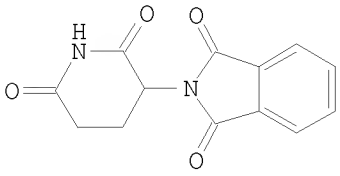


I

AB Metabolite of thalidomide (I) [50-35-1] generated by hepatic microsomes inhibited the attachment of tumor cells to concanavalin A-coated polyethylene. Evidence that metabolite formation is mediated by microsomal cytochrome P 450 [9035-51-2] is presented. Microsomes incubated with I underwent a type I spectral shift. Metabolite formation was reduced or eliminated by CO, SKF-525A [62-68-0], metyrapone [54-36-4], and N-octylamine [111-86-4]. Superoxide dismutase [9054-89-1] treatment had no effect. Metabolite formation required microsomes and NADPH and was dependent on the length of 37° incubation. The metabolite could be isolated by successive hexane and CHCl3 extns. It is likely, the inhibitory I metabolite was

generated by a minor cytochrome P 450 species. Whether this I metabolite is involved in the drug's teratogenic activity remains to be shown.

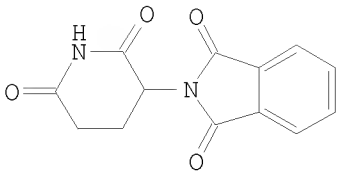
L5 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1984:543568 CAPLUS
DOCUMENT NUMBER: 101:143568
ORIGINAL REFERENCE NO.: 101:21601a,21604a
TITLE: Teratogen metabolism: spontaneous decay hydrolysis products of thalidomide and thalidomide analog are not activated by liver microsomes
AUTHOR(S): Braun, A. G.; Weinreb, S. L.
CORPORATE SOURCE: Dep. Radiat. Ther., Harvard Med. Sch., Boston, MA, USA
SOURCE: Report (1983), DOE/ER/60070-T3; Order No. DE84006117, 18 pp. Avail.: NTIS
From: Energy Res. Abstr. 1984, 9(9), Abstr. No. 17444
DOCUMENT TYPE: Report
LANGUAGE: English
GI



I

AB Thalidomide (I) [50-35-1] and 2 analogs, EM 87 [49785-74-2] and EM 12 [26581-81-7], inhibit the attachment of tumor cells to concanavalin A-coated surfaces only if the drugs are treated with hepatic microsomes and cofactors. Preincubation of these drugs in buffered saline at 37° results in a progressive decline in their ability to be activated to inhibitory products. Similarly, postincubation of the inhibitory products leads to a decline in their ability to inhibit attachment. Decay rates differ for the 3 compds. I, EM 87, and EM 12 require 3, 1, and 6 h, resp., to decline to control levels. These relative rates of decay are consistent with the relative teratogenicity of the 3 drugs.

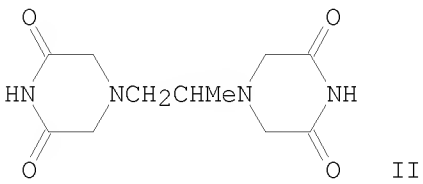
L5 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1981:132131 CAPLUS
DOCUMENT NUMBER: 94:132131
ORIGINAL REFERENCE NO.: 94:21459a,21462a
TITLE: Thalidomide metabolite inhibits tumor cell attachment to concanavalin A-coated surfaces
AUTHOR(S): Braun, Andrew G.; Dailey, James P.
CORPORATE SOURCE: Dep. Radiat. Therapy, Harvard Med. Sch., Boston, MA, 02115, USA
SOURCE: Biochemical and Biophysical Research Communications (1981), 98(4), 1029-34
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB The inhibitory effect of drug treatment on tumor cell attachment to plastic surfaces coated with concanavalin A [11028-71-0] correlated well with the in vivo teratogenicity of the drug. The effects of thalidomide (I) [50-35-1] and some of its metabolites were examined for inhibitory activity. While I and its hydrolysis products did not alter attachment, metabolites of I produced by incubation of the drug with murine liver microsomes were inhibitory. Generation of inhibitory products required the presence of glucose-6-phosphate, NADP, glucose-6-phosphate dehydrogenase, and $MgCl_2$. The degree of inhibition was dependent on the duration of incubation at 37°. These results suggest a model for the teratogenic action of I in which metabolites of the drug alter cell surface function leading to interference with normal morphogenic cell to cell interactions.

L5 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1976:537359 CAPLUS
DOCUMENT NUMBER: 85:137359
ORIGINAL REFERENCE NO.: 85:21963a,21966a
TITLE: Factors related to tumor spread in the body
AUTHOR(S): Boggust, W. A.
CORPORATE SOURCE: Dep. Exp. Med., Trinity Coll., Dublin, Ire.
SOURCE: Advances in Tumour Prevention, Detection and Characterization (1976), 3(Biol. Charact. Hum. Tumours, Proc. Int. Symp., 6th, 1975), 383-90
CODEN: APDCDT
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



II

AB In exts. of human cancers, cathepsins B, C, and D, leucine aminopeptidase [9001-61-0], glucosaminidase [9027-56-9], acid and neutral collagenase [9001-12-1], and fibrinolysin [9001-90-5] activities were found. Collagenase was blocked by the chelating agents dimercaptopropanol (BAL) [59-52-9], EDTA [60-00-4], and o-phenanthroline (I) [66-71-7], and the cytostatic drug ICRF-159 (II) [21416-87-5]. Combinations of I and II were synergistic. II also inhibited cathepsins C and B1 and probably glucosaminidase, but not cathepsin D or leucineaminopeptidase. Mice bearing implanted carcinoma excised on the 10th day, died from lung metastases within 34 days unless otherwise treated. Survival periods were increased by II, but not by I alone. Combinations of I and II substantially increased the survival period. Thus, I and II by acting as enzyme inhibitors and cytotoxic agents they helped to inhibit primary

tumor growth and prevent metastases.

L5 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1970:98435 CAPLUS
DOCUMENT NUMBER: 72:98435
ORIGINAL REFERENCE NO.: 72:17841a,17844a
TITLE: Potentiating effect of thalidomide on methylcholanthrene oncogenesis in mice
AUTHOR(S): Miura, Mitsuhiko; Southam, Chester M.; Wuest, Heinz M.
CORPORATE SOURCE: Sloan Kettering Inst. for Cancer Res., New York, NY, USA
SOURCE: Experientia (1970), 26(3), 305-6
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The i.p. administration of thalidomide (25 mg/day for 5 days in each of 4 consecutive weeks) to mice increased the number of papillomas which developed in response to applications of methylcholanthrene (I) (0.2 ml of a 1% solution for 5 consecutive days) to skin; thalidomide was started 1 week before I and was continued until 1 or 2 weeks after the application of I had stopped. There was no evidence that thalidomide enhanced I oncogenesis via immunosuppression. The oral administration of thalidomide at the same dosage and on the same schedule did not significantly increase the oncogenic response to I.

L5 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:502238 CAPLUS
DOCUMENT NUMBER: 65:102238
ORIGINAL REFERENCE NO.: 65:19127g-h
TITLE: N-Phthaloylglutamimide (thalidomide) in the symptomatic treatment of vomiting
AUTHOR(S): Traldi, A.; Vaccari, G. L.; Davoli, G.
CORPORATE SOURCE: Ist. Patol. Med., Univ., Modena, Italy
SOURCE: Cancro (1965), 18(4), 336-41
CODEN: CAROAF; ISSN: 0008-5480
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB The effectiveness of thalidomide(I) was studied in 14 cancer patients (group 1) with persistent vomiting and in 21 subjects with hemolymphopathy (group 2) in whom vomiting occurred upon intravenous administration of mechlorethamineHCl (II). I was given in a dose of 60 mg. every 8 hrs. to the cancer patients and 60 mg. 0.5 hr. before, and 1 and 4 hrs. after, injection of II to the 2nd group. Antiemetic action was immediate and effective in 9 subjects of the 1st group, and of moderate effectiveness in 3 subjects. In the 2nd group, all 21 patients responded pos., the results being comparable to those obtained with known antiemetics, e.g., phenothiazine and its derivs. I might block afferent impulses of visceral origin, or might interrupt the reflex arc of vomiting in the bulbar centers.

L5 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:108243 CAPLUS
DOCUMENT NUMBER: 64:108243
ORIGINAL REFERENCE NO.: 64:20446a-c
TITLE: Thalidomide and tumor
AUTHOR(S): Mueckter, H.; More, E.
CORPORATE SOURCE: Chem. Gruenenthal G.m.b.H. Stolberg-Rheinland, Germany
SOURCE: Arzneimittel-Forschung (1966), 16(2), 129-34
CODEN: ARZNAD; ISSN: 0004-4172
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The addition of 1% thalidomide to the diet of rats 2 days before intubation

of 20 mg. 7,12-dimethylbenz[α]anthracene (DMBA) delayed both the appearance and growth of DMBA-induced tumors. In rats already infected with DMBA-induced tumors, 1% thalidomide also limited the manifestation and, to a certain extent, growth of the tumors . The curative effect was limited by the size of the tumors at the time of 1st application and by the duration of treatment. Thalidomide had no significant effect on the spontaneously developing, hormone-independent mammary cancer induced by the milk factor virus in C3H/O20 mice. The mechanism of antitumor action of thalidomide differed from the cytostatic action of cyclophosphamide in that thalidomide seemed to exert its effect mainly, or perhaps exclusively, through the endocrine system.

L5 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:30357 CAPLUS
DOCUMENT NUMBER: 64:30357
ORIGINAL REFERENCE NO.: 64:5658d-f
TITLE: Biochemical effects of thalidomide and a histogenetic hypothesis of the malformation of the fetus
AUTHOR(S): Nystrom, Cl.
CORPORATE SOURCE: Univ. Sahlgrenska Sjukhuset, Goteborg, Swed.
SOURCE: International Congress of Chemotherapy, Proceedings (1964), 1963(1), 372-8
CODEN: 14XBAV
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. CA 59, 4441g. Since thalidomide (I) has an N-phthaloylglutamic acid imide structure its possible actions as an antimetabolite against folic acid (II) was investigated. Over 1-3 months, I was administered by injection and orally to 2 patients with tetratoid carcinomas of an embryonal type, presumably with enzyme patterns like that of a fetus. One was a woman of 25 years with an ovarian cancer, the other was a man of 42 with carcinoma of the testes. Blood levels of II were little affected by I. However, I had some effect as an antagonist to II. In doses higher than 3 g./day (as high as 7 g./day), I appeared to interfere with II metabolism as indicated by increased amts. of urinary formiminoglutamic acid. In growth inhibition tests, I did not affect the growth of Streptococcus faecalis or Lactobacillus casei. Hence I did not act as a II antagonist in bacterial growth. For the in vivo human tests, there was an uptake of I by tumor tissue but no particularly marked effects of I on tumor growth. This may perhaps have resulted from the fact that the tumors and their metastases had been treated with heavy doses of ionizing radiations. However, the results suggested that II-dependent tumors might show pharmacotherapeutic responses to I or some of its metabolites. 13 references.

L5 ANSWER 39 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:30356 CAPLUS
DOCUMENT NUMBER: 64:30356
ORIGINAL REFERENCE NO.: 64:5658c-d
TITLE: Effects of cytostatic and tuberculostatic agents in patients with bronchial carcinoma plus active lung tuberculosis
AUTHOR(S): Hammer, O.
CORPORATE SOURCE: Hosp. Falkenstein, Germany
SOURCE: International Congress of Chemotherapy, Proceedings (1964), 1963(1), 209-11
CODEN: 14XBAV
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The mechanisms of action of the title agents are discussed. In combined

treatments, no undue side effects were observed, and no antagonism could be demonstrated between nitrogen mustard derivs. containing an active NCH2CH2 group and antitubercular drugs such as streptomycin or isoniazid. 23 references.

L5 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:29960 CAPLUS
DOCUMENT NUMBER: 64:29960
ORIGINAL REFERENCE NO.: 64:5582b-d
TITLE: Carcinogenesis in tissue culture. III. Effects of the second treatments on 4-dimethylaminoazobenzene-induced proliferating liver cells of normal rats in culture
AUTHOR(S): Katsuta, Hajim; Takaoka, Toshiko
CORPORATE SOURCE: Univ. Tokyo
SOURCE: Japanese Journal of Experimental Medicine (1965), 35(4), 231-48
CODEN: JJEMAG; ISSN: 0021-5031
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. preceding abstract Various second treatments following 4-dimethylaminoazobenzene (I) were given to transform the proliferating cells into malignant cells, including no renewal of culture fluid for prolonged periods and the addition of hormones, I, or thalidomide (II). By no renewal of medium, a slight shift without a definite direction was occasionally produced in the modal number of chromosomes, including one exception which shifted to the tetraploid. When 70 γ growth hormone/ml. was added, the cells did not survive. With 10 γ testosterone/ml., no significant change was induced in cell morphology. The addition of 1 γ I/ml. for 4 days was repeated every 10 days, 1 month, or 1.5 months. Only the cells which received the treatment every 1.5 months survived and proliferated, but little morphological change was observed. The addition of II (10 γ/ml.) temporarily produced giant cells with giant nuclei as well as multipolar mitosis in some of the cell strains. The frequency of such abnormal cells decreased after II was eliminated from the medium. Treated cells were retransplanted into various sites of rats, but no tumors were formed.

L5 ANSWER 41 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1966:14172 CAPLUS
DOCUMENT NUMBER: 64:14172
ORIGINAL REFERENCE NO.: 64:2634b-c
TITLE: Deformations by chemical substances. Experiments on rabbits furnish new results
AUTHOR(S): Gottschewski, Georg H. M.
SOURCE: Umschau in Wissenschaft und Technik (1965), 65(7), 199-203
CODEN: UWTCAZ; ISSN: 0041-6347
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Cyclophosphamide (used for cancer treatment under the name of Endoxan and thalidomide (Contergan) have no effect on specific organs of the fetus. Their effect depends on the time they are administered; it is more pronounced at an early stage because then organs are not yet differentiated and are concentrated in a small area. At later stages of development, however, deformations of individual organs can be produced.

L5 ANSWER 42 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1965:474983 CAPLUS
DOCUMENT NUMBER: 63:74983

ORIGINAL REFERENCE NO.: 63:13855f-g
TITLE: Side effects of anabolic steroids
AUTHOR(S): Suzuki, Hidero; Ogata, Etsuro
CORPORATE SOURCE: Univ. Tokyo
SOURCE: Sogo Igaku (1963), 20, 431-5
CODEN: SOIGAG; ISSN: 0371-1803
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB A review with 15 references.

L5 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1965:39524 CAPLUS
DOCUMENT NUMBER: 62:39524
ORIGINAL REFERENCE NO.: 62:6997c-d
TITLE: Antitumor activity of thalidomide
AUTHOR(S): Gaetani, M.
CORPORATE SOURCE: Ist. Nazl. Studio Tumori, Milan
SOURCE: Giorn. Ital. Chemioterap. (1964), 11(2), 83-6
DOCUMENT TYPE: Journal
LANGUAGE: Italian
AB Daily administration of 500 mg. thalidomide/kg. (I) to tumor-inoculated mice for 14 days had no influence on the normal development of the following tumors: Ehrlich ascites tumor, myeloma Oberling-Guerin-Guerin, sarcoma 180, and transplantable teratoma. This proved to be so for both racemic I and for the pure L(-)-isomer. The body weight and mortality of the mice were not affected by the latter 2 compds.

L5 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:464521 CAPLUS
DOCUMENT NUMBER: 61:64521
ORIGINAL REFERENCE NO.: 61:11213d-h
TITLE: Influence of anticancer agents on the metabolism of δ-aminolevulinic acid in normal and tumor-bearing mice
AUTHOR(S): Hano, Kotobuki; Akashi, Akira
CORPORATE SOURCE: Univ. Osaka, Japan
SOURCE: Gann (1964), 55(1), 25-40
CODEN: GANNA2; ISSN: 0016-450X
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Previous findings had shown that the effect of anticancer agents in restoring lowered enzyme activities in the liver, especially that of catalase, was not always in parallel with their therapeutic effect. To clarify this, the possible inhibitory effect of these agents on heme metabolism, with special reference to Fe, Cu, and δ-aminolevulinic acid (I) metabolism, was investigated in normal and tumor -bearing mice. I dehydratase activity in the liver of tumor bearers was lower than that of normal animals and was very low in tumor cells. Of the anticancer agents tested in vitro, 2,5-bis(ethylenimino)-1,4-benzoquinone and folic acid antagonists inhibited this enzyme in normal mice. On the other hand, carboxamide utilization, in which I is involved with the source of a C1 fragment, occurred at a much higher rate in tumor cells than in the livers of normal and tumor-bearing mice. In the presence of folic acid antagonists, d-catechol, and berberine, carboxamide utilization by tumor cells was markedly inhibited in vitro. Daily decrease in the serum Fe level, blood hemoglobin content, and liver I dehydratase activity was observed after tumor transplantation, at which time serum Cu level increased. Administration of alkylating agents and 8-azaguanine to tumor bearers restored these metabolic

disturbances to normal in parallel with their therapeutic effects. These agents showed no influence on these levels in normal mice. 6-Mercaptopurine, which has a marked anticancer activity with Ehrlich ascites carcinoma, returned the lower liver I dehydratase activity and elevated serum Cu level in tumor-bearing animals to normal. However, the lowered serum Fe level and blood hemoglobin content in tumor bearers were further depressed by treatment with 6-mercaptopurine, and this depressive action was also found in normal mice. Treatment with aminopterin, which was not effective against Ehrlich ascites carcinoma, did not restore the altered metabolism of tumor-bearing animals to normal, and it caused a depression of the blood hemoglobin content in normal mice.

L5 ANSWER 45 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:63728 CAPLUS
DOCUMENT NUMBER: 60:63728
ORIGINAL REFERENCE NO.: 60:11245c-d
TITLE: In vitro test systems for cancer therapy. II. Correlation of in vitro inhibition of dehydrogenase and growth with in vivo inhibition of Ehrlich ascites tumor
AUTHOR(S): DiPaolo, Joseph A.
CORPORATE SOURCE: Roswell Park Mem. Inst., Buffalo, NY
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1963), 114, 384-7
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. Cancer Res. 23, 184-90(1963). Fifteen diverse chemotherapeutic compds. of clin. value as well as those of wide effectiveness in animal tumor systems are shown to give varying responses in vitro. The extent of inhibition by any one compound in vitro ranges from none to significant, depending on the exact in vitro conditions. The dehydrogenase enzyme inhibition test was the most successful on the basis of correlation with extension of survival time of mice bearing the same tumor used in the in vitro studies.

L5 ANSWER 46 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:55507 CAPLUS
DOCUMENT NUMBER: 60:55507
ORIGINAL REFERENCE NO.: 60:9792g-h,9793a
TITLE: Thalidomide-induced alterations in the blastocyst and placenta and the armadillo, Dasypus novemcinctus mexicanus, including a choriocarcinoma
AUTHOR(S): Marin-Padilla, Miguel; Benirschke, Kurt
CORPORATE SOURCE: Dartmouth Med. School, Hanover, NH
SOURCE: American Journal of Pathology (1963), 43(6), 999-1016
CODEN: AJPAA4; ISSN: 0002-9440
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Thalidomide was fed to pregnant armadillos for several days in daily doses of 100 mg./kg. All animals became ill, a majority aborted or failed to implant. Degenerative changes were observed in blastocytes and the trophoblastic columns in the developing placentas. The alterations appeared to have led to fetal bleeding and hematopoietic response. In 1 animal treated during earliest implantation stages an embryo showed asym. phocomelia. This animal developed a widely metastatic choriocarcinoma from the placenta. Embryoid bodies were found in the metastases of the tumor, and endocrine response suggested the presence of chorionic gonadotropin. Only one litter with malformations similar to those seen in man and some exptl. animals was produced. The

reason for this failure was presumably the degree of toxicity resulting in abortions in the first exptl. group and the difficulty in exact timing of the pregnancies. While the dose given exceeded the teratogenic dose reported for man, it was apparent that thalidomide had considerable effect in this species. Its sensitivity to the drug apparently was greater than that of other exptl. animals.

L5 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1964:41422 CAPLUS
DOCUMENT NUMBER: 60:41422
ORIGINAL REFERENCE NO.: 60:7320d-f
TITLE: Treatment of experimental tumors with thalidomide
AUTHOR(S): Pagnini, G.; Di Carlo, R.
CORPORATE SOURCE: Univ. Naples
SOURCE: Bollettino - Societa Italiana di Biologia Sperimentale (1963), 39(22), 1360-3
CODEN: BSIBAC; ISSN: 0037-8771
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The authors produced the Ehrlich ascites carcinoma in 50 white rats by diet and injection. One group of 25 was given thalidomide orally as an aqueous solution at a dosage of 500 mg./kg./day while the 2nd group served as controls. After 10 days some of the animals were sacrificed. The ascitic fluid value was measured and found to be 16.05 ± 2.29 ml. per animal in the treated and 15.66 ± 0.57 ml. per animal in the controls. In another set of rats myeloma was produced by diet and subcutaneous injections, so that in 18 days the pathol. condition existed. One group received orally a dose of aqueous thalidomide at 250 mg./kg./day and was compared with the controls. After 15 days, diameters of the tumors produced were measured and found to be 9.54 ± 2.48 cm.3 per animal and 9.01 ± 1.03 cm.3 in the controls. In both of the above exptl. cases the mortality rate was similar in both the treated and in the controls.

L5 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 1963:424400 CAPLUS
DOCUMENT NUMBER: 59:24400
ORIGINAL REFERENCE NO.: 59:4441g-h,4442a
TITLE: Biochemical effects of thalidomide
AUTHOR(S): Nystrom, C.
CORPORATE SOURCE: Radiotherapy Centre, Goteborg, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1963), 15, 102-3
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Because the chemical structure of thalidomide is related to that of folic acid, there is an enzymic interaction at the one-C-stage. A blocked folio acid action leads to urinary excretion of the intermediary formiminoglutamic acid (I). The amount of I excreted may be regarded as a measure of folic acid antagonism. In vitro microbiol. growth inhibition tests with Lactobacillus easel and Streptococcus faecalis show no folic acid antagonism by thalidomide. Treatment of 2 patients with therapy-resistant teratoid carcinomas in advanced stages showed normal I tests when the daily dose of thalidomide was below 3 g. Doses of 3-7 g. daily showed a marked increase in urinary excretion of I proportional to the dosage. Analysis of tumor tissue revealed thalidomide uptake. It is concluded that folic acid-dependent embryological tumors may be susceptible to thalidomide, and that embryonic germinative epithelium having a high folic acid requirement is deprived of its needs by the biochem. action of thalidomide.

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=> d his

     (FILE 'HOME' ENTERED AT 10:18:31 ON 12 MAR 2009)

     FILE 'REGISTRY' ENTERED AT 10:18:45 ON 12 MAR 2009
                E "THALIDOMIDE"/CN 25
L1              1 S E3

     FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 10:19:17 ON 12 MAR
     2009
L2           8229 S L1
L3           3805 S L2 AND (?CANCER? OR ?TUMOR? OR ?TUMOUR? OR ?NEOPLASM? OR ?LEU
L4            125 S L3 AND (PRD<19930301 OR PD<19930301)
L5             48 S L4 AND (TREAT? OR ADMINIST?)

=>

---Logging off of STN---



=>
Executing the logoff script...


=> LOG Y

COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                              130.99     139.09

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                              -20.50     -20.50

STN INTERNATIONAL LOGOFF AT 10:28:03 ON 12 MAR 2009
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